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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/438,206	11/12/1999	RIYI SHI	7024-427-PUR	9018

26813 7590 02/23/2005

MUETING, RAASCH & GEBHARDT, P.A.
P.O. BOX 581415
MINNEAPOLIS, MN 55458

EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/438,206	SHI ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-30,38-40,43 and 44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-30,38-40,43 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11-24-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 24, 2004 has been entered.

The outstanding rejection under 35 USC 112, first paragraph is withdrawn in view of the Applicant's amendments filed November 24, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-30, 38, 40, and 44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for PEG with 40 to 3500 daltons, does not reasonably provide enablement for PEG 4000. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The instant claims encompass all range of molecular weight of PEG. From the teachings of Shelby, which is provided by the applicant along with the response filed November 24, 2004, it

is known that PEG 4000 would cause dissolution of myelin and may cause manifestation of the loss of neural function. Therefore, in view of the teachings of Shelby, the employment of PEG 4000 is not enabled by the instant specification.

Claims 22-30, 38-40, and 43-44are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 3%- 10% of PEG, does not reasonably provide enablement for 20-40% of PEG. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The instant claims encompass any concentrations of PEG. In view of the teachings of Benzon et al., which is provided by the applicant along with the response filed November 24, 2004, 20-40% of PEG will result in slowing the conduction velocity of the nerve. Therefore, the employment of 20-40% of PEG is not enabled by the instant specification.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 22-29, 38-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application No. 10/132,542. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '542 patent recites the method of treating a mammalian nerve tissue injuries with a biofusion materials. '542 teaches that the preferred biofusion material as polyethylene glycol (See claims 3 and 4 particularly) and the nerve tissue injuries can be spinal cord injuries (See claim 17). One of ordinary skill in the art would have been motivated to employ polyethylene glycol (the preferred agent in '542) in a method to treat spinal cord injuries (the specific recited nerve tissue injury in '542). Employing any preferred biofusion agents, such as polyethylene glycol, would have been reasonably expected to be useful in treating any nerve tissue injuries, including spinal cord injuries.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Applicant's remarks with regard to the double patenting rejection

Applicant's remarks with regard to the outstanding provisional double patenting rejection are acknowledged. The provisional double patenting will be maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22, 24-30, 38-40 and 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balasubramanian (US Patent 5,382,584) in view of Potter et al. (Clin Invest Med, 19(4), Suppl.: S80, #533). Potter is reference of record.

Balasubramanian teaches a method of employing piperazinyl phenylacetamide compounds useful as treatment for spinal cord injuries broadly (see col. 4, line 2). Balasubramanian also teaches one of the routes to administer the piperazinyl phenylacetamide compounds as intrathecal (See col. 5, line 6). Balasubramanian also teaches when administering the piperazinyl phenylacetamide compounds parenterally, such compounds will be formulated into solution or suspension with suitable solvent such as polyethylene glycol 200-1500 (See col. 6, lines 17-27).

Balasubramanian does not expressly teach 4-aminopyridine, a potassium channel blocker, can be combined with method of treating spinal cord injury such as crushed spinal cord injury. Balasubramanian does not expressly teach specifically administering the piperazinyl phenylacetamide compounds with polyethylene glycol 200-1500 intrathecally.

Potter et al. teaches the use of 4-aminopyridine to treat spinal cord injury (See #533).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ 4-aminopyridine with the piperazinyl phenylacetamide compounds of Balasubramanian to treat spinal cord injuries such as crushed spinal cord injury. It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the piperazinyl phenylacetamide with polyethylene glycol 200-1500 intrathecally in a method to treat spinal cord injuries.

One of ordinary skill in the art would have been motivated to employ 4-aminopyridine with the piperazinyl phenylacetamide compounds of Balasubramanian to

treat spinal cord injuries such as crushed spinal cord injury. 4-aminopyridine is known to be useful as treatment for spinal cord injury. The polyethylene glycol containing formulation of Balasubramanian is also known to treat spinal cord injury. Employing them concomitantly for treating the very same condition, spinal cord injuries, would be obvious (*In re Kerkhoven* 205 USPQ 1069).

One of ordinary skill in the art would have been motivated to administer the piperazinyl phenylacetamide with polyethylene glycol 200-1500 intrathecally (Note: a polyethylene glycol containing composition) in a method to treat spinal cord injuries such as crushed spinal cord injury. Since the piperazinyl phenylacetamide compounds of Balasubramanian are known to be useful to treat spinal cord injury. Administering such compounds intrathecally, in solution form with polyethylene glycol 200-1500, to treat spinal cord injury would have been reasonably expected to be effective. It is known that polyethylene glycol is the exemplified solvent useful to dissolve the piperazinyl phenylacetamide compounds of Balasubramanian. Employing polyethylene glycol as the solvent would be considered as selecting from obvious alternatives. The skilled of artisan would possess all conventional administration method of the active compounds such as oral administration. The selection of one or another route of administration would be seen as a simple selection from among obvious alternatives.

Response to Arguments

Applicant's arguments filed November 24, 2004 averring the instant claims relate to methods employing compositions wherein polyethylene glycol is an active have been

considered, but are not found persuasive. Examiner interprets the claims in the broadest and reasonable manner. The herein claims are directed to a method of treating spinal cord injuries comprising polyalkylene glycol. Since the transition phrase "comprising" is recited, the claims do not exclude any ingredients. Therefore, a method of treating spinal cord injuries as herein recited encompasses the method of treating spinal cord injuries by employing any polyethylene glycol containing composition.

Applicant's arguments filed November 24, 2004 averring the cited prior art's failure to teach the effective amount of PEG to restore the nerve impulse conduction have been considered, but are not found persuasive. The arguments are directed to the effects PEG supposed to produce; however, examiner notes that the limitation recited in the claims are directed to the amount of PEG, which is met by the cited prior arts. Therefore, the cited prior arts still render the instant claims obvious.

Applicant's arguments filed November 24, 2004 with regard to the toxicity of PEG, by citing the abstract of Benzon et al., have been considered, but are not found persuasive. Benzon et al. actually studies the alleged toxicity of PEG in epidural and intrathecal administration of PEG containing compositions such as steroids composition. Benzon et al. actually reports that the concentration of PEG plays an important role of the toxicity of PEG. The concentration of 3%, which is equals to the PEG concentration in the steroid products, does not adversely affects the neural functions when epidurally or intrathecally administered. With higher concentrations, such as in the level of 20-40% of PEG, the slowing conduction velocity effect of PEG is more apparent. Benzon et al. also notes that almost anything, including isotonic sodium chloride solution, would

cause adverse effect such as arachnoiditis especially such agents being employed repeatedly (See page 558, col. 1, last paragraph). Therefore, it is clear that mere adverse effects does not teach away or discourage one of ordinary skill in the art to not use PEG in epidural or intrathecal formulation. Since the concentration of the commercial product contains only 3% of PEG 3350, the teachings of Benzon et al. does not teach away or discourage one of ordinary skill in the art not to employ PEG containing composition to treat spinal cord injury.

Applicant's arguments filed November 24, 2004 with regard to the toxicity of PEG, by citing Shelby, have been considered, but are not found persuasive. The formulation Shelby reported contains PEG 4000. However, the formulation cited by the PDR reference is not PEG 4000. It is rather PEG 3350. Therefore, the arguments are not persuasive. Furthermore, there is other study that PEG 3350 been employed and no side effects had been reported (See Benzon et al., page 556, col. 2, first full paragraph).

Applicant's arguments filed November 24, 2004 averring Examiner misapplying *In re Kerkhoven* have been considered, but are not found persuasive. Specially, applicants aver that Kerkhoven does not apply to method claims. Examiner notes that the test is that whether the two components are useful for the same purpose. In the instant case, the PEG-containing composition of Balasubramanian and 4-aminopyridine are useful for the very same purpose (i.e., treating spinal cord injury). Therefore, combining them together and employing them for treating the very same disorder (spinal cord injury) would be considered obvious, absent evidence to the contrary. In

the instant case, no such evidence is seen herein. Therefore, the instant claims are seen to be properly rejected under 35 USC 103(a).

New ground of rejection

Claims 22-30, 38-40, and 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shulman (US Patent 4,599,354) in view of Edwards (US Patent 4,369,769).

Shulman teaches a extended epidural pain relief composition containing 2.3% of PEG 3600 or with molecular weight of 1000-5000 (See col. 3, lines 32-42). Shulman also teaches this is preferably selecting the PEG that is non-toxic in a concentration required to perform the suspending function (See col. 6, lines 64-68).

Shulman does not expressly teach the epidural pain relief composition as useful in treating spinal cord injury.

Edwards teaches that spinal cord fracture and injury always cause pain (See col. 7, lines 22-32).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the PEG containing composition of Shulman in the treatment of spinal cord fractures and injury.

One of ordinary skill in the art would have been motivated to employ the PEG containing composition of Shulman in the treatment of spinal cord fractures and injury. It is known that severe spinal cord injury and fracture lead to pain. Therefore, administering the composition of Shulman epidurally would have been reasonably

expected to be effective in relieving one of the symptoms of spinal cord fracture such as pain since the composition of Shulman is known to produce prolonged pain relief. Therefore, employing the composition of Sulman as one of the spinal cord injury treatment regimen would be considered obvious and reasonably expected to be useful.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Primary Examiner
Art Unit 1617